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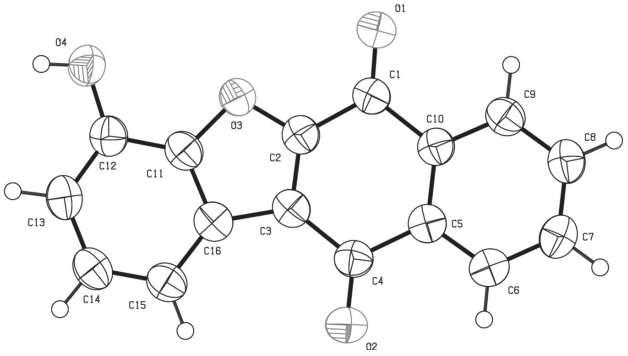

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Abstract

$C_{16}H_8O_4$, monoclinic, *Pc* (no. 7), $a = 3.7133(1)$ Å, $b = 9.7214(4)$ (2) Å, $c = 15.5765(6)$ Å, $\beta = 96.121(2)°$, $V = 559.08(3)$ Å^3, $Z = 2$, $R_{gt}(F) = 0.0506$, $wR_{ref}(F^2) = 0.1274$, $T = 150(2)$ K.

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The crystal structure is shown in the figure. Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

Source of materials

To a solution of 2,3-dichloronaphthalene-1,4-dione (0.5 g, 2.2 mmol) in pyridine (analytical pure, 99%, 50 mL), 3,3′′,4′′,5,7-pentahydroxy-flavone (0.67 g, 2.2 mmol) was added and heated to 80 °C with magnetic stirring. After 24 h, the reaction mixture was cooled to room temperature and

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Table 1: Data collection and handling.

Crystal:	Red block
Size:	0.40 × 0.15 × 0.10 mm
Wavelength:	Cu $K\alpha$ radiation (1.54178Å)
μ:	0.95 mm^{-1}
Diffractometer, scan mode:	Bruker APEX-II, φ and ω-scans
θ_{max}, completeness:	74.7°, >99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	4922, 1904, 0.024
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 1848
$N(param)_{refined}$:	182
Programs:	Bruker programs [1], SHELX [2, 3]

Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2).

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
C1	0.2574(8)	0.9446(3)	0.0871(2)	0.0482(7)
C2	0.1782(8)	0.7996(3)	0.1059(2)	0.0490(7)
C3	0.0003(8)	0.7091(3)	0.0505(2)	0.0479(6)
C4	−0.1447(8)	0.7502(3)	−0.0370(2)	0.0490(7)
C5	−0.0726(8)	0.8956(3)	−0.0610(2)	0.0481(7)
C6	−0.1944(8)	0.9418(3)	−0.1436(2)	0.0509(7)
H6	−0.3165	0.8801	−0.1841	0.061*
C7	−0.1391(9)	1.0769(4)	−0.1672(2)	0.0565(8)
H7	−0.2233	1.1071	−0.2238	0.068*
C8	0.0375(9)	1.1678(3)	−0.1091(2)	0.0564(8)
H8	0.0720	1.2607	−0.1254	0.068*
C9	0.1643(9)	1.1232(3)	−0.0268(2)	0.0516(7)
H9	0.2887	1.1855	0.0129	0.062*
C10	0.1111(8)	0.9885(3)	−0.0022(2)	0.0469(6)
C11	0.1807(9)	0.6079(3)	0.1763(2)	0.0494(7)
C12	0.2476(9)	0.5100(3)	0.2423(2)	0.0510(7)
C13	0.1155(9)	0.3793(3)	0.2219(2)	0.0542(7)
H13	0.1524	0.3086	0.2640	0.065*
C14	−0.0704(9)	0.3483(3)	0.1413(3)	0.0554(7)
H14	−0.1572	0.2574	0.1306	0.067*
C15	−0.1317(9)	0.4455(3)	0.0769(2)	0.0531(7)
H15	−0.2559	0.4228	0.0223	0.064*
C16	−0.0040(8)	0.5787(3)	0.0952(2)	0.0503(7)
O1	0.4319(7)	1.0189(2)	0.13825(16)	0.0583(6)
O2	−0.3184(7)	0.6724(2)	−0.08651(16)	0.0589(6)
O3	0.2932(5)	0.7437(2)	0.18328(14)	0.0496(5)
O4	0.4307(7)	0.5496(2)	0.31748(16)	0.0580(6)
H4	0.4757	0.4806	0.3492	0.087*

diluted with 250 mL of water and the resulting precipitate was obtained *via* filtration. After drying, the precipitate was separated on a Biotage Isolera Four flash column chromatography system (SNAP Cartridge KP–Sil 10 g), being eluted with the mobile phase consisting of hexane/ethyl acetate (from 100:0 to 90:10, v/v), to give a red product. This product was mixed with equal molar ratio of NaOH, extracted by water and concentrated to achieve a solid. The solid material was further crystallized in glacial acetic acid to furnish a red colored single crystal suitable for X-ray analysis. The melting point of this crystal was determined as 536 K using a XT-4 melting point instrument (Beijing Taike Instrument Co., Ltd, Beijing, China). NMR spectra were performed on a DRX-400 Bruker NMR spectrometer (Bruker, Germany). **^{1}H-NMR** (400 MHz, DMSO-*d6*) δ: [ppm] 8.14∼8.17 (2H; m), 7.91∼7.93 (2H; m), 7.62∼7.64 (1H; d, J = 7.8 Hz), 7.35∼7.39 (1H; t, J = 7.9 Hz), 7.10∼7.12 (1H; *d*, J = 7.8 Hz); **^{13}C-NMR** (101 MHz, DMSO-*d6*) δ: [ppm] 181.7, 175.4, 153.9, 145.4, 144.3, 134.9, 134.6, 133.4, 132.6, 127.7, 126.8, 126.7, 124.5, 124.1, 115.7, 113.4. **IR** (ν_{max}, cm^{-1}): 3395, 2920, 2851, 2519, 1668, 1654, 1634, 1593, 1575, 1559, 1492, 1377, 1341, 1320, 1289, 1227, 1183, 1145, 1040, 975, 904, 840, 774, 708. **ESI-MS**: 263.0[M−1]$^-$; **ACPI-MS**: 265.0[M+1]$^+$, 263.0[M−1]$^-$.

Experimental details

H atoms bonded to C and O atoms were positioned geometrically with d (O—H) = 0.90 Å, d(C—H) = 0.95 Å (aromatic CH), and treated as riding atoms. For all H atoms, isotropic displacement parameters were calculated as $U_{iso}(H) = 1.2\ U_{eq}(C)$ and $U_{iso}(H) = 1.5\ U_{eq}(O)$. No chiral carbon is present in the title structure and the Flack parameter 0.50(9) suggests the presence of a racemic twin refinement of inversion twinning giving a twin ratio of 0.6(3).

Comment

The naphthofuranoquinone core is an integral part of various anticancer products such as benzonaphthofurandione analogs [4], in which the furan ring forming on the naphthoquinone core can significantly increase these anticancer activities [5]. The naphthofuranoquinone scaffold was constructed mainly based on base-catalyzed condensation reaction between 1,4-naphthoquinone and the corresponding phenol [6, 7], and intermolecular C—C-bond formation and intermolecular *O*-alkylation were believed to be two successive steps [8]. Other preparation methods by light irradiation [9] or oxidation [10] provided some evidences for explaining this condensation process. The attempt to synthesize a fused naphthofuranoquinone compound derived from a condensation reaction between 1,4-naphthoquinone and 3,3″,4″,5,7-pentahydroxy-flavone resulted in an unexpected novel derivative. The synthesis of the title compound involves an elimination reaction of the C6—C3 group from the flavone moiety under basic conditions. This elimination reaction mechanism was hitherto unknown and very interesting, and necessitates further investigation. The crystal structure analysis confirmed the formation of 4-hydroxynaphtho [2,3-*b*]benzofuran-6,11-dione as the product. The title crystal structure is built up by $C_{16}H_8O_4$ molecules, in which all geometric parameters are within normal ranges. There is an intramolecular hydrogen bond: O4—H4···O2 (d(O4—H4···O2) = 2.733(2) Å; α(O4—H4···O2) = 167.4°). During a database search for the molecular core scaffold, two crystal structure were found namely. 2,4-di-*tert*-butylbenzo*b*] naphtho[2,3-d]furan-6,11-dione [11] and dinaphtho[2,1-b.2′,3′-d]furan-8-13-dione [12].

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References

1. Bruker. APEX3, SAINT-Plus, XPREP. Bruker AXS Inc., Madison, WI, USA (2016).
2. Sheldrick, G. M.: SHELXT – integrated space-group and crystal-structure determination. Acta Crystallogr. **A71** (2015) 3–8.
3. Sheldrick, G. M.: Crystal structure refinement with SHELXL. Acta Crystallogr. **C71** (2015) 3–8.
4. Rhee, H. K.; Kwon, Y.; Chung, H. J.; Lee, S. K.; Choo, H. Y. P.: Synthesis, cytotoxicity and topoisomerase II inhibitory activity of benzonaphthofurandiones. Bull. Korean Chem. Soc. **32** (2011) 2391–2396.
5. Morello, A.; Pavani, M.; Garbarino, J. A.; Chamy, M. C.; Frey, C.; Mancilla, J.; Guerrero, A.; Repetto, Y.; Ferreira, J.: Effects and mode of action of 1,4-naphthoquinones isolated from *Calceolaria sessilis* on tumoral cells and *Trypanosoma parasites*. Comp. Biochem. Physiol. **112C** (1995) 119–128.
6. Cheng, C. C.; Dong, Q.; Liu, D. F.; Luo, Y. L.; Liu, L. F.; Chen, A. Y.; Yu, C.; Savaraj, N.; Chou, T. C.: Design of antineoplastic agents on the basis of the 2-Phenylnaphthalene-type structural pattern. 2. synthesis and biological activity studies of benzo[*h*]naphtho[2,3-*d*] furan-6,l 1-dione derivatives. J. Med. Chem. **36** (1993) 4108–4112.
7. Crawford, P. W.; Gross, J.; Lawson, K.; Cheng, C. C.; Dong, Q.; Liu, D. F.; Luo, Y. L.; Szczepankiewicz, B. G.; Heathcock, C. H.: Electrochemical properties of some biologically active quinone derivatives: furanquinones, pyridoquinones, and diplamine, a cytotoxic pyridoacridine alkaloid. J. Electrochem. Soc. **144** (1997) 3710–3715.

8. Sartori, M. F.: Heterocyclic quinones from 2,3-dichloro-1,4-naphthoquinone. Chem. Rev. **63** (1963) 279–296.
9. Hiroshi, S.; Atsushi, K.; Hideo, S.; Hiroki, M.; Toshihiro, T.; Hisanori, S.; Masao, T.; Kazuhiro, K.: Photoinduced molecular transformations. Part 156. New photoadditions of 2-hydroxy-1,4-naphthoquinones with naphthols and their derivatives. Tetrahedron. **51** (1995) 1377–1386.
10. Takeya, T.; Kondo, H.; Otsuka, T.; Tomita, K.; Okamoto, I.; Tamura, O.: A novel construction of dibenzofuran-1,4-diones by oxidative cyclization of quinone-arenols. Org. lett. **9** (2007) 2807–2810.
11. Suzuki, M.; Imai, K.; Wakabayashi, H.; Arita, A.; Johmoto, K.; Uekusa, H.; Kobayashi, K.: Photorearrangements in spiro-conjoined cyclohexa-2,5-dien-1-one. Tetrahedron **67** (2011) 5500–5506.
12. Farrugia, L. J.; Scott, C. F.; Peacock, R. D.: A Naphthofuranoquinone. Acta Cryst. **C52** (1996) 1310–1311.